Elevated serum glial fibrillary acidic protein (sGFAP) is associated with increased risk of neuromyelitis optic spectrum disorder in the N-MOmentum randomised, masked, placebo-controlled clinical trial of inebilizumab


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INTRODUCTION

Neuromyelitis optica spectrum disorder (NMO) is a severe autoimmune disease characterised by recurrent inflammation of the optic nerve, spinal cord, brain or brainstem.1 2 In patients with NMO, aquaporin-4, a water channel protein that is expressed on astrocytes, is frequently targeted by autoantibodies, which causes the selective destruction of astrocytes (figure 1).3 4 This results in increased concentration of glial fibrillary acidic protein (sGFAP), an intermediate filament protein predominantly expressed by astrocytes, in serum and cerebrospinal fluid following astrocyte destruction.5 6 sGFAP is a biomarker of neuroaxonal damage and can be monitored in serum at frequent intervals to assess disease activity.7 8 In clinical trials of patients with NMO, aquaporin-4 antibody titres displayed a good correlation with the extent of astrocyte destruction and the volume of damaged tissue.9 10 NMO-IgG expression has also been linked to increased disability in patients with NMO regardless of treatment.11 12 In patients with NMO, sGFAP concentration increased during adjudicated NMO attacks but was reduced in those with minor adjudicated attacks compared with patients receiving placebo (p = 0.048) (figure 6).13

In the N-MOmentum study, inebilizumab treatment was associated with decreased sGFAP concentration compared with participants receiving placebo (p = 0.001) (figure 3).14 This is consistent with the observation that adjudicated attacks in NMO patients are associated with increased sGFAP concentration (figure 2).13 In the current study, patients were monitored prospectively for serum sGFAP levels to assess the relationship between sGFAP concentration and adjudicated NMO attack severity (figure 3).15

CONCLUSIONS

In the N-MOmentum study, inebilizumab treatment was associated with a decreased risk of adjudicated NMO attacks compared with placebo, in patients with normal or elevated sGFAP concentrations at baseline. Patients with NMO had increased sGFAP concentration compared with patients in the HD and the RRMS reference cohorts. sGFAP concentration increased significantly within 1 week of an adjudicated attack and correlated with adjudicated NMO attack severity. sGFAP concentrations during adjudicated NMO attacks were lower in inebilizumab-treated patients than in those receiving placebo (p = 0.048) (figure 6). sGFAP concentration increased normally but not significantly during adjudicated attacks in inebilizumab-treated patients (figure 3). These observations suggest that sGFAP could be a clinically useful biomarker of disease activity and increased attack risk in NMO.